Remarks

Amendments in the Specification

The specification was amended at page 21, lines 23-24, and page 30, line 5 to delete the hypertext.

The specification was also amended to clarify the descriptions of Tables 1 and 2. Support for the amendments come from Tables 1 and 2, and SED ID NOs: 7-40, 42-177, and 179-192 which are amino acid sequences, and SEQ ID NO: 41, 178, 193, and 194 which are nucleic acid sequences.

No new matter is added by way of these amendments.

Amendments in the Claims

Claim 114 was amended to recite that the recombinant viral vector comprises a viral capsid fusion protein comprising a protein transduction domain operably linked to an organelle localization signal. Support for the amendment is found throughout the specification, for example on page 20, lines 6-23, and page 9, lines 21-26.

Claim 117 was amended to depend from claim 116 and to recite that the fusion protein is expressed on the exterior surface of the bacteriophage. Support can be found throughout the specification for example on page 9, lines 22-26, and page 20, lines 6-23.

Claim 119 was amended to correct antecedent basis in view of amendments to claim 114.

Claim 128 was amended to clarify the claim language.

New Claims

New claims 129-139 are introduced.

Support for claims 129, 131, 134 and 136 is found in the specification at least on page 21, lines 5-20.

Support for claim 130 and 135 is found at least on page 19, lines 21-25 and page 38, lines 16-19.

Support for claim 132 and 137 is found at least on page 32, lines 9-12.

Support for claim 133 is found throughout the specification, for example on page 20, lines 6-23, Example 1 and Figures 1B and 1C.

Support for claim 138 is found at least on page 20, lines 6-23.

Support for claim 139 is found throughout the specification, for example on page 20, lines 6-23, Example 1 and Figures 1B and 1C.

Election/Restrictions

Applicant acknowledges the Examiner's withdrawal of the restriction requirement between linking groups I and II, and rejoinder of claim 116. Claims 114, 116-118, 121, 128, and new claims 129-139 are pending.

Objections to the Specification

Applicants amended the title of Table 1 and the paragraph after Table 2 to delete the hyperlinked text. In view of these amendments, the objection is moot. No new matter was introduced.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 114, 116, 117-119, 121, and 128 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Examiner rejected the claims for reciting "one or more of the viral capsid proteins comprise an organelle localization signal," because it is unclear how one protein can comprise another protein. Without making any admissions, and solely to facilitate prosecution, Applicant amended claim 114 to recite a viral capsid fusion protein. Withdrawal of the amendment is respectfully requested.

Rejection Under 35 U.S.C. § 103

Claims 114, 116-119, 121, and 128 were rejected under 35 U.S.C. § 103(a) as being obvious over Nakanishi, et al., *Curr. Protein Peptide Sci.*, 4:141-150 (2003), in view of Del Gaizo, et al., *Mol. Ther.*, 7:720-30 (2003). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Legal Standard

The starting point for an obviousness determination must be the Supreme Court's decision in *KSR v. Teleflex,* 550 U.S. 398 (2007), which refocuses the determination of whether a claimed invention is obvious back to the process the Court had defined in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966). There, the Court had held that the obviousness determination should address four factors, all of which must be considered, though not in any

prescribed order: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any secondary considerations suggesting nonobviousness, such as commercial success, failure of others, and long felt but unmet need. *Id.* The Court cautioned that the fact finder should be careful about reading the teachings of the invention at issue into the prior art, to avoid applying inappropriate hindsight, *ex post* reasoning. *Id. at 36.*

Analysis

(a) The scope of the cited art

Nakanishi, et al., *Curr. Protein Peptide Sci.*, 4:141-150 (2003) "Nakanishi"

Nakanishi allegedly describes viral vectors including lambda phage particles displaying a protein transduction domain. Nakanishi also allegedly describes viral vectors including lambda phage particles displaying a nuclear localization signal. Nakanishi does not describe viral vectors including lambda phage particles displaying a protein transduction domain ***and*** a nuclear localization signal.

Del Gaizo, et al., *Mol. Ther.*, 7:720-30 (2003) "Del Gaizo"

Del Gaizo allegedly describes a non-viral fusion protein including a protein transduction domain, a mitochondrial localization signal, and GFP. Del Gaizo is not directed to viral vectors at all, let alone viral vectors including lambda phage capsid proteins which display a protein transduction domain operably linked to an organelle localization signal.

(b) Ascertaining differences between the cited art and the claims

Pursuant to 37 C.F.R. § 1.131, Applicant submits a declaration under 37 C.F.R. § 1.131 by inventor Dr. Shaharyar Khan. In the declaration, Dr. Khan describes how he engineered various plasmids to express a fusion protein construct including one or more of four elements: a protein transduction domain, an organelle localization signal, viral capsid protein, and GFP (see paragraphs 3-5, and 7). The Examiner's attention is drawn particularly to paragraph 7 which describes a construct including a TAT protein transduction domain, ***and*** a mitochondrial localization signal, ***and*** the viral capsid protein gpD. The construct was expressed in competent cells, and the resulting fusion protein was recovered. The fusion protein was mixed with commercially available lambda packaging extract to generate a viral vector including the viral capsid fusion protein (paragraph 8). When the fusion protein and packaging extract are mixed with a polynucleotide, the vector packages the polynucleotide for delivery to a subcellular organelle. In this way, Dr. Khan conceived and reduced to practice the claimed viral capsid fusion protein including an organelle localization signal and protein transduction domain, as well as a viral vector containing the viral capsid fusion protein prior to March 31, 2003.

Applicant submits that in view of the declaration, Nakanishi, et al., *Curr. Protein Peptide Sci.*, 4:141-150 (2003), which was published in April of 2003, is not prior art to the above-referenced application. Furthermore, Nakanishi does not describe all of the elements of the claims. For example, Nakanishi does not describe a viral vector including all three of the

claimed elements. Nakanishi does not describe a construct including a protein transduction domain, ***and*** an organelle localization signal, ***and*** a viral capsid protein.

Applicant also submits that in view of the declaration, Del Gaizo, et al., *Mol. Ther.*, 7:720-30 (2003), which was published in June of 2003, is not prior art to the above-referenced application. Furthermore, Del Gaizo does not teach all the elements of the claims. As discussed above, Del Gaizo is directed to ***non-viral*** fusion proteins. Del Gaizo is not directed to polynucleotide delivery vectors, let alone viral vectors. Del Gaizo does not teach or suggest viral capsid proteins, therefore Del Gaizo does not teach or suggest viral capsid fusion proteins including a protein transduction domain and an organelle localization signal which can be used to encapsulate polynucleotides and deliver them to subcellular organelles.

For at least these reason, the claims are non-obvious over the cited art. Withdrawal of the rejection under 35 U.S.C. § 103 is respectfully requested.

Allowance of claims 114, 116-119, 121, and 128-139 is respectfully solicited.

Respectfully submitted,

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